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ABSTRACT

Objectives. Sulfamethoxazole/trimethoprim (SMX/TMP) has been considered as the first-line therapy for the treatment of *Pneumocystis jirovecii* pneumonia (PCP), which is not an uncommon opportunistic infection seen in systemic rheumatic disease (SRD) patients receiving glucocorticoids and immunosuppressants in Japan. For the treatment of active PCP, the recommended dosage is 75 to 100 mg/kg of SMX and 15 to 20 mg/kg of TMP per day given for 14 to 21 days.

However, the high burden of adverse drug reaction of generally recommended high-dose SMX/TMP and the limited evidence regarding optimal dose of SMX/TMP from clinical studies constrains its use. In this multicenter retrospective study, we reviewed consecutive patients with SRD receiving immunosuppressive therapy who developed PCP and were treated with SMX/TMP as an initial anti-pneumocystis agent and evaluated effectiveness and safety of lower dose SMX/TMP therapy by comparing these patients originally divided into three groups according to the initial dosage of SMX/TMP.

Methods. We compared effectiveness and safety of SMX/TMP for the treatment of PCP among patients divided into three groups according to the initial dosage of SMX/TMP: the low, ≤10 mg/kg/day; the intermediate, 10-15 mg/kg/day; and the high and conventional, 15-20 mg/kg/day for TMP dose.

Results. Eighty-one patients, including 22, 30, and 29 patients in the low-, the intermediate- and the high-dose group could be analyzed and the 30-day survival rate were 100%, 93.3%, and 96.7%, respectively (P=0.28). There were significant dose-dependent increasing trends of severe adverse drug reactions (ADRs) for SMX/TMP that were graded as ≥ 3 according to the Common Terminology Criteria for Adverse Events. When stratified by presence of severe hypoxemia defined by alveolar-arterial O2 gradient ≥45mmHg, the 30-day survival and treatment modification rate were similar among the three groups, but frequency of severe ADRs were significantly decreased in the low-dose group. The low-dose group was independently and negatively associated with treatment modification within 14 days and severe ADRs.

Conclusions. Lower dose SMX/TMP therapy with ≤10 mg/kg/day for TMP was as effective as higher dose therapy for the treatment of PCP and associated with lower rates of treatment modification and severe ADRs in patients with systemic rheumatic diseases.